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EXAMINER

PAK, YONG D

ART UNIT PAPER NUMBER

1652

DATE MAILED: 03/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/035,918

Applicant(s)

SHAH ET AL.

Examiner

Yong D. Pak

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-8 and 10-54 is/are pending in the application.
- 4a) Of the above claim(s) 25-43 and 48-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-8,10-24 and 44-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

In view of the Appeal Brief filed on December 7, 2005, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing at the end of this Action.

Claims 1, 3-8, 10-54 are pending. Claims 25-43 and 48-54 are withdrawn.
Claims 1, 3-8, 10-24 and 44-47 are under consideration.

Response to Arguments

Applicant's amendment and arguments filed on December 7, 2005, have been fully considered and are deemed to be persuasive to overcome the rejections previously

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applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claim 19 is objected to because the name of the organisms recited in the claim should be italicized.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 3-8, 10-24 and 44-47 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter.

Claims 1, 3-8, 10-24 and 44-47, as written, is directed to non-statutory subject matter. Claims 1, 3-8, 10-24 and 44-47 are drawn to methods using a host cell still attached to a host such as a human being. The claims do not make it clear that the cell, even though it is a recombinant cell, is an isolated cell. Claims that read on a human being are considered non-statutory. Examiner suggests amending the claim to recite "an isolated host organism..." to overcome the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and claims 3-8, 10-24 and 44-47 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "determining whether the colonies contain active glucose oxidase comprises: measuring a concentration of the glucose oxidase". It is not clear to the Examiner as to how those skilled in the art can conclude that colonies have active glucose by measuring the concentration of glucose oxidase. This is because the concentration of "glucose oxidase" can be measured in many different ways (for e.g. using antibodies) and such measurements do not always indicate whether said enzyme is active. Measuring the concentration of glucose in the presence and absence of glucose oxidase provides information on whether "glucose oxidase" is active. Further, it is not clear to the Examiner how the concentration of the glucose oxidase is measured from the colonies unless the glucose oxidase is first isolated. Therefore, the claim lacks essential steps: isolation step and assaying of the glucose oxidase. Examiner requests clarification of the claimed method.

Claim 1 and claims 3-8, 10-24 and 44-47 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 recites the phrase "desirable properties" and "desired peroxide resistant properties". The metes and bounds of these phrases in the context of the

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above claims are not clear to the Examiner. A perusal of the specification did not provide the Examiner with a specific definition for the above phrases. Therefore, the metes and bounds of what is "desirable" or "desired" are not clear. Examiner requests cancellation of the above phrases

Claims 3, 5 and 10 and claims 11-18 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 5 and 10 recite the term "functionality". The metes and bounds of this term in the context of the above claims are not clear to the Examiner. A perusal of the specification did not provide the Examiner with a specific definition for the above term. Therefore, it is not clear to the Examiner either from the specification or from the claim as to what specific "functions" of glucose oxidases are encompassed in the term "functionalities". Examiner requests clarification of the above term.

Claims 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-8 recite the phrase "determining whether the colonies have active glucose oxidase". It is not clear to the Examiner as to how those skilled in the art can conclude that colonies have active glucose oxidase by only measuring fluorescence or by using a substance that changes color in the presence of active glucose oxidase.

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This is because in the claimed method, applicants have not set up any control steps. Therefore, the method lacks essential step(s). Examiner requests clarification of the claimed method.

Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 recites the phrase "the host is a host organism". The metes and bounds of this phrase in the context of the above claim are not clear to the Examiner. Claim 1, from which claim 44 depends from, recites using a "host organism". Therefore, it is not clear to the Examiner how the "host organism" recited in claim 44 differs from the "host organism" recited in claim 1. Examiner requests clarification of the above phrase.

Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47 recites the phrase "accelerated test environment". The metes and bounds of this phrase in the context of the above claim are not clear to the Examiner. A perusal of the specification did not provide the Examiner with a specific definition for the above phrase. Therefore, it is not clear to the Examiner either from the specification or from the claim as to what test environments are encompassed in the above phrase. Examiner requests clarification of the above phrase.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5, 12-24 and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valdes et al., Stemmer and Hatzinikolaou et al.

Claims 1, 3-5, 12-24 and 44-45 are drawn to a method of formulating or producing mutant glucose oxidases by obtaining a library of glucose oxidase genes, creating a library of mutated glucose oxidase genes by the methods recited in claims 20-24, introducing each mutated glucose oxidase genes into separate expression vectors, inserting said vectors into host organisms recited in claim 19, growing colonies

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of the host organism, determining whether the colonies contain active glucose oxidase by the methods recited in claims 3-8, 10-18 and 45-47 and determining whether the colonies are resistant to peroxide and then measuring the concentration of the glucose oxidase.

Valdes et al. (cited previously on form PTO-892) discloses that glucose oxidase in glucose sensors are degraded by peroxide and this "decay can lead to the eventual failure of the sensor" (abstract and page 367). Valdes et al. teaches that to ensure longer sensor functionality, instead of replacing the sensor with fresh enzyme, as has been practiced in the art, techniques to "prevent the degradation of the enzyme" is advantageous (page 375). With this teaching at hand, one having ordinary skill in the art would conclude that glucose oxidase may be prevented by using chemical agents, as suggested by Valdes et al. or to use glucose oxidase mutants that are resistant to peroxide since methods of generating mutants having resistance to chemicals are known in the art, as discussed below. Valdes et al. also teaches a method of determining activity of glucose oxidase (page 370).

The difference between the reference of Valdes et al. and the instant invention is that the reference of Valdes et al. does not teach a method of producing mutant glucose oxidase that is resistant to degradation from peroxide. However, there are many methods widely available in the art of creating mutant genes by random mutations and screening for mutants displaying desired functional properties, such as having resistance to a chemical, such as a peroxide.

Stemmer (US Patent 6,117,679 – form PTO-892) discloses a method of producing mutant enzymes by obtaining a library of genes of interest, creating a library of mutated genes by multiple cycles (at least 2-6 cycles) of PCR, error-prone PCR and/or gene shuffling (abstract, Column 4-11 and Column 22). In the method of Stemmer, each mutated genes are introduced into separate expression vectors, which are then inserted into *E. coli* (Column 25, 31-32). Stemmer teaches these host cells are then tested for the presence of desired mutations, such as growing the cells or colony under selective pressure and isolating the protein and testing of the protein encoded for activity (Column 32). Stemmer teaches a method of screening for colonies having resistance to a chemical by plating transformed cells comprising mutated genes onto agar plates having varying concentrations of said chemical (Column 78).

Hatzinikolaou et al. (form PTO-892) discloses a library of glucose oxidase genes known in the art, such as *A. Niger* (page 371). Hatzinikolaou et al. also discloses a method of isolating and purifying glucose oxidase as recited in claims 14-18 and methods of measuring glucose oxidase activity and concentration of glucose oxidase (pages 372-373).

Therefore, combining the teachings of Valdes et al., Stemmer and Hatzinikolaou et al., it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to formulate or produce mutant glucose oxidases having resistance to peroxide by generating a library of mutated genes using the glucose oxidase gene of Hatzinikolaou et al. and the method of Stemmer, transforming *E. coli* with vectors comprising each of the mutated genes, growing colonies of said cells and

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determining whether the colonies have active glucose oxidase and then determining whether the colonies or the glucose oxidase comprised in the colony are resistant to peroxide. One of ordinary skill in the art would have been motivated to do so in order to generate active glucose oxidases that are resistant to peroxide. One of ordinary skill in the art would have been motivated to produce mutant peroxide resistant glucose oxidases in order to use them in glucose sensors, thereby prolonging their use, since Valdes et al. teaches that glucose oxidases in glucose sensors are degraded by peroxide, leading to failure of the sensor. One of ordinary skill in the art would have had a reasonable expectation of success since Hatzinikolaou et al. teaches glucose oxidase genes, Stemmer teaches a method of generating a library of mutant genes and screening for activity and other desired properties, such as resistance to a chemical.

Therefore, the above references render claims 1, 3-5, 12-24 and 44-45 *prima facie* obvious.

Claims 6-8, 10-11 and 46-47 rejected under 35 U.S.C. 103(a) as being unpatentable over Valdes et al., Stemmer and Hatzinikolaou et al. as applied to claims - 5, 12-24 and 44-45 above, and further in view of Wagner.

Claims 6-8, 10-11 and 46-47 are drawn to a method of formulating or producing mutant glucose oxidases by obtaining a library of glucose oxidase genes, creating a library of mutated glucose oxidase genes, introducing each mutated glucose oxidase genes into separate expression vectors, inserting said vectors into host organisms, growing colonies of the host organism, determining whether the colonies contain active

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glucose oxidase by testing glucose oxidase in sensors and using fluorescence of a leuco-cryalsta-violet, and determining whether the colonies are resistant to peroxide.

Valdes et al., Stemmer and Hatzinikolaou et al. in combination teaches a method of formulating or producing mutant glucose oxidases, as discussed above.

The difference between the reference of Valdes et al., Stemmer and Hatzinikolaou et al. and the instant invention is that said references do not teach a method of determining whether the colonies contain active glucose oxidase by testing glucose oxidase in sensors and using fluorescence.

Wagner (EP 0 251 475 A1 - form PTO-892) discloses a method of determining glucose oxidase activity via a sensor by measuring fluorescence emission from a dye, wherein oxidation of glucose by active glucose oxidase reduces the fluorescence emission (pages 2-3). In the method of Wagner, the glucose oxidase is conjugated to a dye and immobilized in the sensor (page 3). Wagner also teaches that any fluorescent dye sensitive to quenching of its fluorescence emission by oxygen can be used (page 5).

Aldrich Catalog (cited previously on form PTO-892) discloses a leuco-cryalsta-violet dye (page 1005).

Therefore, combining the teachings of Valdes et al., Stemmer and Hatzinikolaou et al., Wagner and Aldrich Catalog, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use the method of Wagner to ascertain activity of the glucose oxidase, wherein glucose oxidase is isolated and purified by the method taught by Hatzinikolaou et al. One of ordinary skill in the art

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would have been motivated to do so in order to determine whether the colonies comprising mutated glucose oxidases have active glucose oxidase. One of ordinary skill in the art would have had a reasonable expectation of success since Wagner teaches how to determine activity of glucose oxidase by measuring fluorescence emission from a dye, wherein oxidation of glucose by active glucose oxidase reduces the fluorescence emission.

Therefore, the above references render claims 6-8, 10-11 and 46-47 *prima facie* obvious.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.


Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652



Manjunath Rao

Primary Patent Examiner 1652



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